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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,372	06/08/2006	Frank Schilke	4385-053939	9406

28289 7590 08/23/2010

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EXAMINER	
FUBARA, BLESSING M	
ART UNIT	**PAPER NUMBER**
1613	
MAIL DATE	**DELIVERY MODE**
08/23/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,372	SCHILKE ET AL.	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/11/2010; 6/01/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The examiner acknowledges receipt of IDS filed 03/11/2010 and 06/01/2010 and request for reconsideration filed 06/01/2010. No claim is amended. The new claims 7-16 filed 1/12/2006 are pending.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 7-16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Shaffner (US 5,980,573) in view of Fox, Jr. et al. (US 5,019,096) and further in view of Neis et al. (US 5,997,544) and Kirschner et al. (US 5,942,218) for reasons of record and reiterated herein.

5. Claims 14-16 were inadvertently omitted in the title of the rejection but were addressed in the body of the rejection. For example, claims 13-15 and 16 were addressed on page 4, paragraph 10 of the last office action of 03/01/2010.

6. Shaffner describes the use of antibiotic impregnated bone cement comprised of polymethylmethacrylate (PMMA) to prevent the formation and spread of infection (see column 2, lines 4-6. 54, 55).

7. Furthermore, Fox teaches that medical devices for external or internal uses are known to introduce bacterial, viral, fungal or other undesirable infection (see column 1, lines 14-16 of Fox, Jr.) and Fox, Jr. proposes incorporating antimicrobial agents such as silver salt and chlorhexidine biguanide to produce infection resistant medical device (see column 2, lines 24-27, 35-41).

8. Bone cements containing additives such as antimicrobial agent/antibiotic agent are also known in the art (see column 6, lines 34-39 of Nies) and the antibiotic agents are used in amounts of 5% to 20% (see Neis at column 6, line 49).

9. Also, Kirschner discloses that polyhexamethylene biguanide is used as wound antiseptic in amounts of 0.001-0.05% (see the abstract).

10. Shaffner teaches the critical element of incorporating antibiotic agent into PMMA to prevent the spread of infection so that the method of claim 7 is met; but Shaffner does not name any specific antibiotic or antimicrobial agent for inclusion into the PMMA. But Fox teaches incorporating biguanide into medical devices so that the medical devices would resist bacterial, viral and/or fungal infection. The specific biguanide disclosed by Fox is chlorhexidine.

11. Also, Neis uses 5-20% antibiotic agent in bone cement; and Kirschner uses polyhexamethylene biguanide in amounts of 0.001-0.05. Chlorhexidine and polyhexamethylene

biguanide are both biguanides as evidenced by column 6, lines 6 and 7 of Khan et al. (US 6,046,143).

12. The %amount of the biguanide in Kirschner at 0.001-0.05 is a narrower range than the amount of active in claims 10, 14 and 15 thereby meeting the limitations of these claims and for claims 7 and 11, one having ordinary skill in the art would select a specific amount of the biguanide that would provide the anticipated resistance to microbial infection. The polyhexamethylene biguanide of Kirschner meets the limitation of the biguanide of claims 7, 11 and 16. The PMMA bone cement of Shaffner meets the PMMA of claims 7 and 13-15. For claim 8, since polyhexamethylene biguanide is the recited antimicrobial agent, the limitation of claim 8 is met when polyhexamethylene biguanide is used. For claims 9 and 13, the recitation that PMMA does not adversely affect the wound healing process is the property of the PMMA and the PMMA of Shaffner would also not adverse affect the wound healing process and in fact, Shaffner has not described the PMMA as having adverse effect on wound healing. The prosthesis implant of Shaffner meets claim 12

13. Therefore, one having ordinary skill in the art at the time the invention was made would have incorporated antimicrobial agents such as chlorhexidine and polyhexamethylene biguanide in the PMMA of Shaffner to prevent the formation and spread of infection according top the combined teachings of Shaffner, Fox, Nies and Kirschner. When using polyhexamethylene biguanide as the antimicrobial agent, one having ordinary skill in the art at the time the invention was made would have been motivated to use the biguanide in amounts of form 0.001 to 0.05 since these amounts have been shown by Kirschner to be effective as antiseptic.

14. Prior art of Interest:

15. Polymethylmethacrylate bone cement is a known product for use in orthopedic surgery or in artificial dentures (see the whole document of HAAS, with emphasis on the abstract, second full paragraph of left column of page 380).

16. No claim is allowed.

Response to Arguments

17. Applicant's arguments filed 06/01/2010 have been fully considered but they are not persuasive.

18. In the paragraph bridging pages 3 of 8 and 4 of 8, applicant refers to the examination guidelines of 1) Determining the scope and content of the prior art; 2) Ascertaining the differences between the claimed invention and the prior art; and 3) resolving the level of ordinary skill in the pertinent art; for determining obviousness under 35 USC 103 in vi9ew of the Supreme Court Decision in KSR International Co. v. Teleflex Inc.

19. Response: The three factors are not the only factors according to the decision in the KSR case. However, in determining the obviousness of the claims over the cited prior art, a determination of the scope of the scope and content of the prior art was made, the differences between the prior art and the examined claims were noted and it was resolved that the ordinary skilled artisan had adequate guidance to use the known biguanide of the claims in the bone cement of Shaffner to prevent and stop the formation and spread of infection since chlorhexidine (FOX) and polyhexamethylene biguanide (Kirschner) are known antiseptic biguanides effective for controlling microbial growth according to Fox and Kirschner.

20. Applicant argues on page 5 of 8 that none of the cited references suggests or discloses the use of polyhexamethylene biguanide in bone cement.

21. Response: The examiner agrees that the cited prior art does not teach the use of polyhexamethylene biguanide in bone cement, but the rejection combined references that in combination render obvious the use of polyhexamethylene biguanide in the bone cement of Shaffner since the critical element is controlling microbial growth in the bone cement with antiseptic agents such as chlorhexidine (Fox) and polyhexamethylene biguanide (Kirschner) known in the art to control microbial growth.

22. Applicant also agues on page 5 of 8 that the combination of the cited references would not provide a method according to claim 7.

23. Response: The examiner disagrees. The method of claim 7 prevents microbial colonization in polymethyl methacrylate (PMMA) bone cement by admixing the PMMA with polyhexamethylene biguanide; the %amount of the polyhexamethylene biguanide is less than 1%. Similarly, Shaffner impregnates PMMA with antibiotic agent to prevent the formation and spread of infection, Fox teaches that antimicrobial agent such as chlorhexidine are incorporated into medical devices in order that the medical device would resist infection; Chlorhexidine is a biguanide and Kirschner teaches that polyhexamethylene biguanide is used as a wound antiseptic; and polyhexamethylene biguanide and chlorhexidine are biguanides known to control microbial growth and Neis teaches incorporating antibiotic in bone cement; each of Shaffner, Fox, Kirschner and Neis incorporate antibiotic or antimicrobial agent into a medical device or bone cement so that the combination of the teachings would motivate the incorporation of the antibiotic of Shaffner or Neis and the antiseptics of Fox or Kirschner into the bone cement and expect that the these compounds would effectively inhibit or prevent microbial growth in the bone cement.

24. On pages 5 of 8 to 7 of 8 of the remarks, applicant argues that the core of the invention is a bone cement having an antiseptic compound that is released by diffusion without the addition of a further additive; and that the antiseptic within the bone cement prevents colonization of the surface of the bone cement with bacteria, and that it was unexpected that low amounts of the high molecular weight polyhexamethylene biguanide (abbreviated by applicant as PHMBG) in amounts of up to 1 wt% combined with PMMA was released in effective amount during a long term range of more than 7 days to effectively suppress colonization of the bone cement with bacteria, and that this effect was comparable to gentamicin and applicant referred to Figs. 1A and 1B of the application showing the unexpected result and also that, the prevailing opinion is that small, water soluble molecules are preferred for release form solid polymeric carrier materials by diffusion. Therefore applicant contends that it would not have been obvious to use polyhexamethylene biguanide in place of chlorhexidine in bone cement in view of the high antiseptic effectiveness polyhexamethylene biguanide (PHMBG), a compound having a different molecular design, and in view of the surprising release of the polyhexamethylene biguanide from bone cement that was not disclosed or obvious from Kirschner.

25. Response: The presence of Figs. 1A and 1B in the specification will be addressed below as it applies to the manner of presenting Figures/Drawings. Figure 1A looks at the effect of 0.077% and 0.155% polyhexamethylene biguanide (PHMBG) on "germ count" and the effect of 0.86% gentamicin on "germ count" after elution while Fig. 1B looks at the same effect but the Fig. uses different scale on the germ count/cm^2 axis. Thus the following issues with the data in Figs. 1A and 1B do not in any way support applicant's argument that polyhexamethylene biguanide (PHMBG) cannot be used in place of chlorhexidine with the PMMA bone matrix. i)

the data does not look at release of polyhexamethylene biguanide (PHMBG) from PMMA or from solid polymeric carrier materials by diffusion; the comparison is between polyhexamethylene biguanide (PHMBG) and gentamicin, and on page 3 of the specification, the data says that 0.155% by weight of polyhexamethylene biguanide (PHMBG) in PMMA bone cement is as effective in preventing colonization as 0.86 % by weight of gentamicin; ii) the specification has not disclosed that there was a long standing problem to be solved or unsolved with regards to the delivery of polyhexamethylene biguanide (PHMBG) from solid polymeric carrier materials by diffusion.

26. Furthermore, the assumption by applicant that "antiseptic effect of PHMBG is not exclusively based on the simple release of the compound into the surrounding media and the destruction of the suspended" is not a factual showing that polyhexamethylene biguanide (PHMBG) cannot be used in place of chlorhexidine in PMMA. Further also, the amount that shows similar prevention of colonization as gentamicin is 0.155% while amount in claim 7 is 1% or less and ranges are claimed in claims 10 and 13-15.

27. Therefore, claims 7-16 are obvious over the combination of references cited in that polyhexamethylene biguanide (PHMBG) can be used in place of chlorhexidine in PMMA bone cement according to the rejections on record.

28. Applicant's reference to Figs. 1A and 1B in the specification:

29. Applicant has brought to the examiner's attention that there are drawing figures in the specification. Guidance on the arrangement of the elements of the application is provided by 37 CFR 1.77 where the elements appear in the order:

(1) Utility application transmittal form.

(2) Fee transmittal form.

(3) Application data sheet (see § 1.76).

(4) Specification.

(5) Drawings.

(6) Executed oath or declaration.

30. The manner of making drawings must comply with the requirements of 37 CFR 1.81, 1.83, 1.84 ; see also MPEP 601, 608 with emphasis on 608.01 [R-7], VI (ILLUSTRATIONS IN THE SPECIFICATION), 608.01(f) (BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S): See also MPEP § 608.01(f) (A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74). Applicant is also requested to follow the guidelines provided by 37 CFR 1.84.

31. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

32. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on Monday to Thursday from 7 a.m. to 5:30 p.m.

33. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

34. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Blessing M. Fubara/
Primary Examiner, Art Unit 1618